Analysis of Primary Pancreatic Cancer Trends in Oroville Area, 1988–2005

Cancer Surveillance Section
Cancer Surveillance and Research Branch
California Department of Public Health
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BACKGROUND

In late May 2007, the Cancer Registry of Northern California (Region 6 of the California Cancer Registry [CCR]) received a concern about pancreatic cancer in the Oroville area. Oroville is a city in Butte County, in the Chico metropolitan area, with a population of approximately 13,000 in the 2000 decennial census. In the 2000 census, approximately 77% of residents were white, 7% Asian/Pacific Islander, 4% black, and 4% Native American/Alaska Native; among all race groups, approximately 8% of residents were of Hispanic ethnicity. The concern addressed in this report originated with a local citizen who reported 24 cases of pancreatic cancer being diagnosed or dying during the previous year, and who was concerned that these cases were linked to a chemical fire in 1987 at the Koppers wood treatment facility, located one-quarter mile south of the Oroville city limits. The federal Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Health Investigations Branch (EHIB) of the California Department of Public Health both conducted environmental assessments in the area after the Koppers fire.

As a routine part of its assessment, ATSDR worked with CCR to look at cancer incidence in the Oroville area. At the time of the assessment, the Registry could only analyze data for 1988 and 1989. The CCR evaluation showed no increased risk of cancer in the area, but noted that, "Cancers, if any, may

not be observed for several years following the time of exposure," suggesting that it would be advisable for CCR to redo its analysis in the future.[1]

In considering the epidemiology of primary pancreatic cancer, the most important risk factor is increasing age. Incidence increases exponentially with age; median age at diagnosis in the United States is 72 years. There are also sex differences in risk, with men experiencing approximately 50% higher risk than women. Race/ethnic comparisons show that in the U.S., blacks have higher age-adjusted incidence rates (AAIR) than whites; during 1996–2000, AAIRs were 10.2 and 6.6 per 100,000 in blacks and whites, respectively. Genetic factors play an important role, with approximately 10% of cases attributable to inherited genetic disorders. A diagnosis of diabetes is also associated with increased risk. Meta-analyses in 1995 and 2005 found that a diagnosis of diabetes for at least five years was associated with a relative risk (RR) of 2.0 for pancreatic cancer.

Many studies have found a relationship between certain environmental exposures and cases of pancreatic cancer, including personal cigarette smoking, environmental tobacco smoke, and chemical exposures. The most consistent of these environmental risk factors is cigarette smoking. RR estimates have ranged from 2.0 to 6.0. Data show a decreasing risk with time since smoking cessation (clear reduction after 10 years), possibly supporting a late-stage effect of smoking.

Overweight and obesity are associated with a small to moderate increased risk for pancreatic cancer. Overall, the data suggest an increased risk for pancreas cancer associated with meat consumption, possibly due to heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs) formed with high temperature cooking. Overall, the preponderance of the evidence suggests a lower risk of pancreas cancer is associated with a diet that includes more fruits and vegetables, but the association is not confined to specific foods. Previously reported associations between pancreatic cancer risk and coffee and alcohol consumption are now considered to be due to confounding.

The association of occupation and workplace exposures and pancreas cancer has been extensively studied, but results have been variable and the strength of association is estimated to be small. Among these studies, however, the most suggestive and seemingly consistent associations include those between pancreas cancer and chlorinated hydrocarbons, the PAH/nitrosamine complex, and the pulp and paper industry.[2–7] One study showed an increased risk of pancreatic cancer with polychlorinated biphenyl (PCB) exposure, with a latency period of 10 or more years.[8]

Thus, the present analysis was undertaken in response to citizen concern about potentially elevated incidence of primary pancreatic cancer in the Oroville area, and represents a follow-up to the earlier CCR analysis from around 1990. For the present analysis, data were available for 18 years, from 1988 to 2005. Data for 2006 are not yet available due to the time required for all cases to be reported to the Registry and verified.

Typically, community concerns about cancer clusters are referred to CCR for initial assessment. If CCR finds an elevation in cancer incidence that is unlikely to have occurred by chance, and if there are concerns that environmental exposures could have contributed, CCR policy is to refer the issue to EHIB for review of environmental concerns.

METHODS

For the present analysis, we began with all incident cases of primary invasive pancreatic cancer (SEER site recode 21100) that were diagnosed in CCR Region 6 between 1988 and 2005. Region 6 includes the counties of Butte, Colusa, Del Norte, Glenn, Humboldt, Lake, Lassen, Mendocino, Modoc, Napa, Plumas, Shasta, Siskiyou, Sonoma, Tehama, and Trinity. Because tissue biopsy is necessary to distinguish primary from secondary pancreatic tumors in patients with prior non-pancreatic

malignancies, we included: 1) all cases where pancreatic cancer was the first malignancy; and 2) all cases where pancreas cancer was the second or higher malignancy, if the case was microscopically confirmed. We used age/sex/race-specific incidence rates for all 16 counties in Region 6 to compute the expected number of cases (E) for each year, and cases from Butte County census tracts 0025.00 through 0033.00 to obtain the observed number (O) for the Oroville area. (Please see attached map for location of census tracts.) Specifically, using 19 standard U.S. Census Bureau age groups and five race/ethnic groups (white, black, Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native), we computed 190 separate age/sex/race-specific incidence rates for the population of Region 6 for each year. For each year, we multiplied each of these Region 6 incidence rates (R_i) by the estimated population of the Oroville area in that age/sex/race group (n_i), and then summed the products to obtain values of E, i.e. $E = \sum R_i \times n_i$.

CCR staff derived annual population estimates for the Oroville area census tracts, based on age/sex/race-specific population counts from the 1990 and 2000 U.S. decennial censuses; data for intercensal years were derived assuming linear changes in population. To confirm the accuracy of this assumption, we compared our intercensal estimates for the Oroville area (all age/sex/race groups combined) with 1990–2007 figures from the California Department of Finance (DOF) for the total population within the Oroville city limits. The slope of the population change from our linear model was in excellent agreement with the slope seen in the DOF estimates (approximately 1% increase in population per year). In the 2000 decennial census, the population for the census tracts examined in this report was 44,041.

FINDINGS

To examine whether the incidence of primary pancreatic cancer appeared to be changing over time, we first conducted preliminary analyses examining observed and expected counts for every year from 1988–2005 (Figure 1). Figure 1 shows that from 1988 to 2003, the number of observed cases (*O*) fluctuated around the number of expected cases (*E*), with *O* above *E* in some years and below *E* in others. As seen in the figure, there were more years where *O* was below *E*. In 2004 and 2005, the number of observed cases was greater than the expected number, and greater than the number of observed cases seen in previous years.

Based on these preliminary results, we conducted our main Poisson analysis based on two-year intervals, beginning with 1988–1990 and ending with 2004–2005 (Table 1). In accordance with current CCR policy, we compared *O* and *E* by computing a 99% Poisson confidence interval (CI) around *O*, and determining whether *E* fell into this interval. Table 1 shows that in all of the time intervals prior to 2004–2005, there were no statistically significant differences between *O* and *E* at the 99% confidence level. However, during 2004–2005, the number of cases observed was nearly twice the number expected (23 versus 11.95; SIR = 1.92), and this difference was statistically significant at the 99% confidence level.

Because small areas can have large variations in cancer incidence over the short term, CCR often performs analyses over a longer term, specifically, the most recent five years of data. Thus, we also conducted an analysis using data from 2001 to 2005. During this 5-year period, *O* = 41 and *E* = 30.19 (SIR = 1.36). In this 5-year analysis, *E* fell within the 99% CI around *O* (26.38–60.56).

DISCUSSION

Between 1988 and 2003, the number of observed cases of pancreatic cancer in the Oroville area was approximately equal to the number of expected cases. However, in 2004–2005, the number of observed cases was nearly the twice the expected number. The reasons for this elevation in incidence are unclear. The difference between observed and expected cases is significant at the 99% confidence level over the last two years of available data, but not over the last five years of available data. It is not clear whether the significant elevation in cancer incidence seen in the last two years of data is transitory, or will continue into the future. In order to accurately determine the public health significance of this recent increase, it will be critical to continue monitoring pancreas cancer incidence in the Oroville area using CCR surveillance data. As more data become available, CCR epidemiologists will examine whether the number of observed cases remains high, or returns within the expected range.

There are many limitations when applying these methods to investigate cause-effect relationships in small area analyses. Apart from concerns of environmental exposures, other possible explanations for the elevated cancer incidence include: chance; unmeasured local differences in the prevalence of risk factors for pancreatic cancer, e.g. smoking and diabetes; and potential errors in estimating population counts for non-census years.

In considering the role of chance, it must be noted that cancer is a much more common condition than many people realize. In the U.S., nearly 1/2 of all men and more than 1/3 of all women will develop cancer during their lifetime. Consequently, groupings of cancer cases in the same geographic area can and often do occur by chance alone. For example, if a computer randomly assigns 100 dots to a grid with 100 squares, some squares will have several dots and some will have no dots. In the same way, many reported “cancer clusters” are actually random groupings of cancer cases that happen to occur in the same time and place.

Another point to consider is that the development of cancer is a multi-step process, often taking many years between tumor initiation and growth to a clinically diagnosable cancer. Thus, some former residents may be diagnosed with cancer after moving out of an area, and some new residents will be diagnosed shortly after moving into an area, without these geographic patterns reflecting any relevant environmental exposure.

CONCLUSIONS/RECOMMENDATIONS

Although this analysis has attempted to account for local differences in the age, sex, and race distribution of the population, it is often difficult to provide a comprehensive explanation for a group of cancer cases. CDPH will be working with the Butte County health department and the local community to determine, if possible, what factors may have contributed to the elevated levels of pancreatic cancer in the area in 2004-2005.

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Figure 1. Observed vs. Expected Cases of Primary Pancreatic Cancer in Oroville Area, 1988−2005

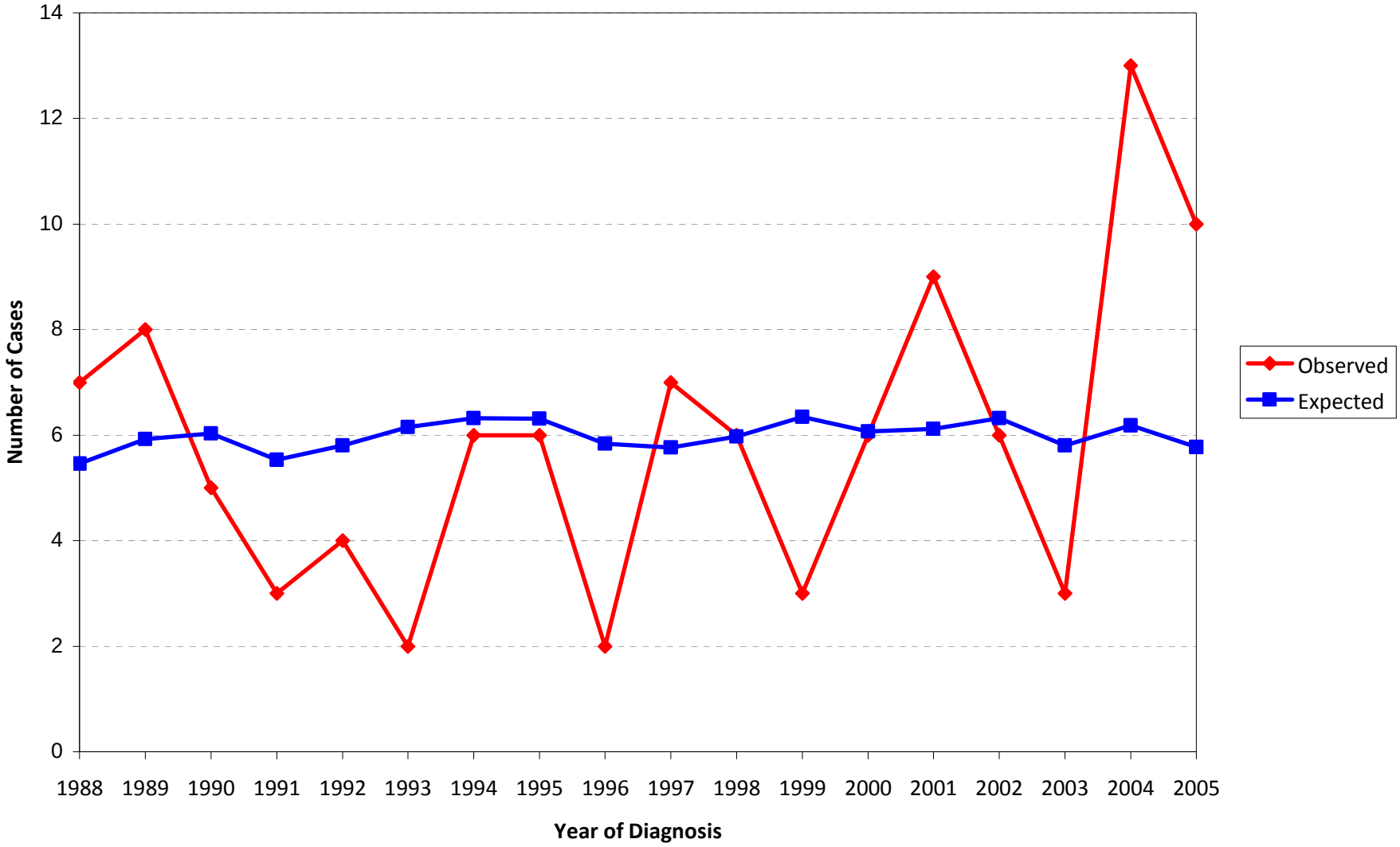

Table 1. Poisson Analysis of Surveillance Data — Primary Pancreatic Cancer, Oroville Area, 1988–2005

Time Period	Observed Cases (99% CI)	Expected Cases	Standardized Incidence Ratio (99% CI)
1988-89	16 (7.57–29.48)	11.39	1.40 (0.66–2.59)
1990-91	8 (2.57–18.58)	11.56	0.69 (0.22–1.61)
1992-93	7 (2.04–17.13)	11.96	0.59 (0.17–1.43)
1994-95	12 (4.94–24.14)	12.64	0.95 (0.39–1.91)
1996-97	11 (4.32–22.78)	11.60	0.95 (0.37–1.96)
1998-99	9 (3.13–20.00)	12.31	0.73 (0.25–1.62)
2000-01	16 (7.57–29.48)	12.19	1.31 (0.62–2.42)
2002-03	11 (4.32–22.78)	12.12	0.91 (0.36–1.88)
2004-05	23 (12.52–38.48)	11.95	1.92 (1.05–3.22)

Abbreviation: CI, confidence interval.

Oroville City Limits and Associated Census Tracts